anti-MIF antibody binds to the 12.5 kDa human MIF consisting of the amino acid sequence of SEQ ID NO: 5.

Please add the following new claims:

-- 73. (New). The diagnostic method of Claim 66 wherein, the patient is known or suspected to be suffering from a condition or disease caused by cytokine-mediated toxicity.

74. (New) The diagnostic method of Claim 73, wherein said condition or disease caused by cytokine-mediated toxicity is selected from the group consisting of endotoxin-induced septic shock, endotoxin-induced toxic shock, shock, inflammatory diseases, graft versus host disease, autoimmune diseases, acute respiratory distress syndrome, granulomatous diseases, chronic infections, transplant rejection, cachexia, asthma, viral infections, parasitic infections, malaria, and bacterial infections. --

REMARKS:

Claims 66-68 are pending, and stand rejected. By this amendment, Claim 66 has been amended and new Claims 73 and 74 have been added (Claims 69-72 having been cancelled previously), leaving Claims 66-68 and 73-74 pending.

Applicants have amended the claims to point out more clearly that which they consider to be their invention, and to claim preferred embodiments. Thus, Claim 66 has been amended to clarify that "the anti-MIF antibody binds to the 12.5 kDa human MIF consisting of the amino acid sequence of SEQ ID NO: 5". Support for this amendment is provided, for instance, at page 10, line 3, as amended in the preliminary amendment filed with the instant application on April 25, 2000, indicating that the amino acid sequence of human T cell MIF of the invention is listed in the Sequence Listing at SEQ ID NO: 5. New Claims 73 and 74 are directed to preferred

embodiments of the diagnostic method of the invention in which the patient is known or suspected to be suffering from a condition or disease caused by cytokine-mediated toxicity (Claim 73), particularly such a condition listed in Claim 74. Support for these claims is provided, for instance, at page 44, lines 13-27. Applicants also note that these embodiments of the condition or disease caused by cytokine-mediated toxicity are also recited in the patented method of treatment claims of related U.S. Patent No. 6,080,407, based on the same disclosure as here.

Since no new matter is added and this Amendment is believed to place the claims as a whole in condition for allowance, or at least in better form for consideration on appeal, in that this amendment only corrects an informality and directs claims to preferred embodiments believed to be free of the outstanding rejection and otherwise patentable, entry and consideration of this amendment after final rejection is considered proper and is respectfully requested.

Applicants appreciate the indication by the Examiner that Claims 66-68 are free of all previous rejections.

Claims 66-68 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting the term "having" instead of "comprising" or "consisting of" in Claim 66. Claim 66 has been amended to replace the cited term "having" with the suggested term "consisting of", which is considered appropriate for the recited amino acid sequence of the specified polypeptide.

Accordingly, Applicants believe that the present amendment overcomes the objection and rejection of Claims 66-68 under 35 U.S.C. § 112, second paragraph and therefore this rejection may properly be withdrawn.

All outstanding objections and rejections having been fully addressed, Applicants believe that the instant claims as presently amended are free of the cited art and otherwise in condition for allowance, and early notice to that effect is respectfully requested.

Applicants note, however, that the instant Office Action was dated June 24, 2002, after Applicants filed an Information Disclosure Statement (IDS) on May 10, 2002, citing international patent publication WO 90/11301. Applicants request that the Examiner consider this document and so indicate by returning to Applicants an initialed copy of the Form-1449 filed with the above IDS.

Applicants also wish to bring to the attention of the Examiner an additional Information Disclosure Statement submitted herewith, disclosing a document that has recently come to the attention of present counsel for Applicants, namely U.S. Patent No. 5,786,168 to Ishizaka, et al. which issued on an application filed May 31, 1995 and claims priority of several earlier cases. Applicants request that this document be considered and made of record by the Examiner, and that the Examiner so indicate by returning an initialed copy of the accompanying Form PTO-1449.

Submission of this document is not intended as an admission that Ishizaka, et al. is available as prior art against the present claims. However, applicants would like to direct the Examiner's attention to the following in Ishizaka, et al.: "The entire nucleotide sequence of full length cDNA (PNY 106) is shown in FIG. 2. The sequence was homologous to the sequence of a purported human MIF cDNA (Weiser, et al., Proc. Natl. Acad. Sci. U.S.A. 86: 7522-7526 (1989), except that the codon from nucleotides 390 to 392 is AAT (asparagine) in GIF cDNA, whereas the MIF cDNA has a codon of AGT (serine)" (column 33, lines 36-43); and text sections concerning monoclonal antibodies (column 26, line 1 - column 27, line 21; and column 42, line 66 - column 43, line 2).

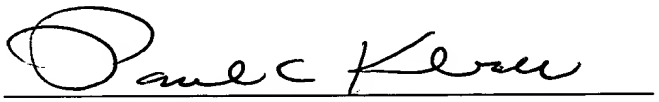
Applicants nevertheless believe that Ishizaka, et al., taken alone or in combination with any of the documents cited in the present rejection, would not teach or suggest, either inherently

or otherwise, a monoclonal anti-MIF antibody of the presently amended claims, that neutralizes biological activity of the specified MIF polypeptide.

If any issues remain to be addressed in this matter, which might be resolved by discussion, the Examiner is respectfully requested to call Applicants' undersigned counsel at the number indicated below.

Respectfully submitted,

PIPER RUDNICK LLP



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MARKED-UP COPY OF AMENDED CLAIMS

66. (Twice Amended) A diagnostic method for determining the amount of MIF protein in a patient, comprising:

(a) obtaining a bodily fluid sample from the patient; and

(b) determining the amount of MIF in the sample using an immunoassay with an anti-MIF antibody, wherein the immunoassay is selected from the group consisting of ELISA, immunoprecipitation, immunohistocytochemistry, and Western analysis, and wherein MIF is a human MIF polypeptide having a molecular weight approximately 12.5 kDa, and wherein the anti-MIF antibody binds to the 12.5 kDa human MIF [having] consisting of the amino acid sequence of SEQ ID NO: 5.